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IN THE U.S. PATENT AND TRADEMARK OFFICE

Applicant: Koichi ITO et al.

For: Heterodiazinon Compound

Serial No.: 09/913 444

Group: 1624

Filed: August 15, 2001

Examiner: Bruck Kifle

Attorney docket

No.: 0425-0847P

The Commissioner of Patents and Trademarks

Washington, D.C. 20231

DECLARATION UNDER 37 CFR 1.132

I, Takahisa HANADA, declare as follows:

I am one of the co-inventors of the invention as claimed and described in the instant patent application. I have carried out additional tests, procedures and results of which are described below.

Inhibitory action on AMPA-inducing inflow of calcium into nerve cells

The test was carried out in the same way as shown in the instant patent application, except for using compounds shown in the hereto attachment. The compounds shown as Sample No. 074, 125, 163, 187 and 188 fall within the claimed invention of the instant application. The compounds shown as Sample No. 044, 045, 048, 068, 114 and 132 fall within the disclosure of the cited US-A 4 670 555 to Dekeyser et al.

As test results, Sample No. 074, 125, 163, 187 and 188 of the claimed invention of the instant application provided IC_{50} (μM) of 11.8, 1.10, 2.28, 4.14 and 11.10, respectively, and Sample No. 044, 045, 048, 068, 114 and 132

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of US-A 4 670 555 to Dekeyser et al provided IC_{50} (μ M) of more than 100, as are shown in terms of IC_{50} (μ M) in the hereto attachment.

It is noted from the test data that the invention compounds are superior to the cited prior art in view of the inhibitory action on AMPA-inducing inflow of calcium into nerve cells.

I hereby declare that all statements made herein of any own knowledge are true, and that all statements made on information and belief are believed to be true; and further, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United State Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Dated: June 12, 2000

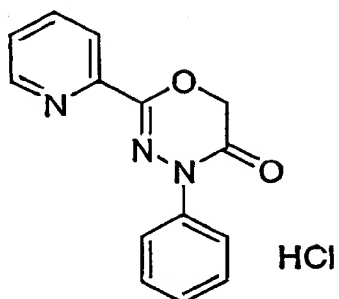
Takahisa Hanada

Takahisa HANADA

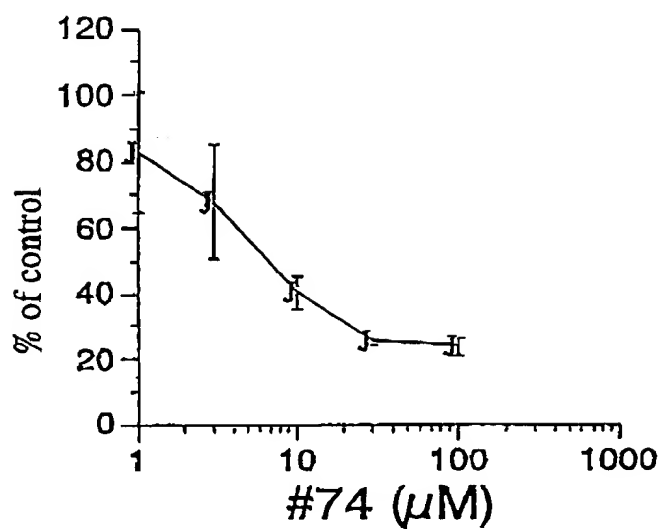
Attachment: 6 sheets

Sample No. 074

Structure

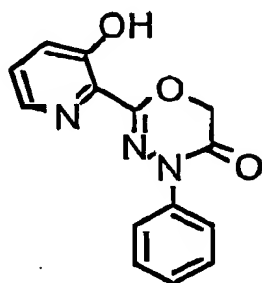


MW 289.72

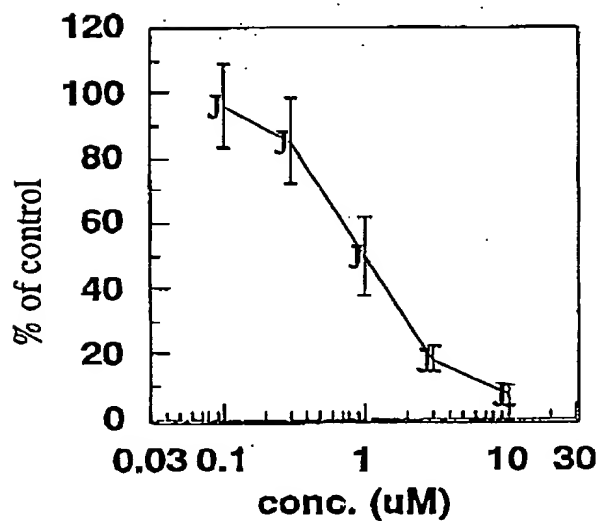
Ca²⁺[Ca²⁺]_i (IC₅₀, μM) 11.8

Sample No. 125

Structure

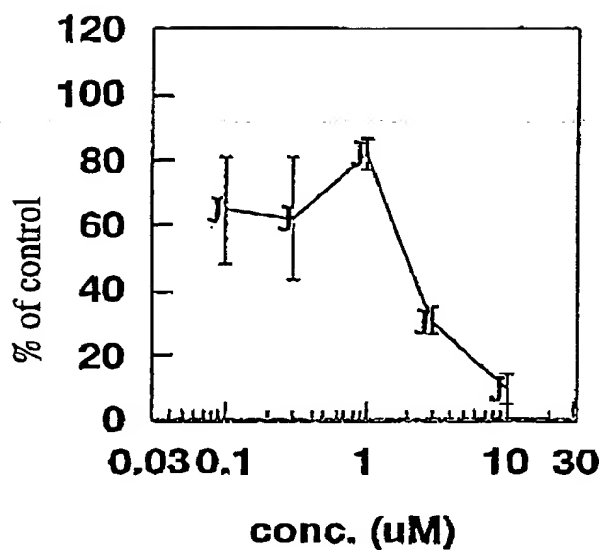
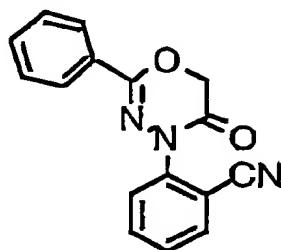


MW 269.26

Ca²⁺[Ca²⁺]_i (IC₅₀, μM) 1.10

Sample No. 163

Structure

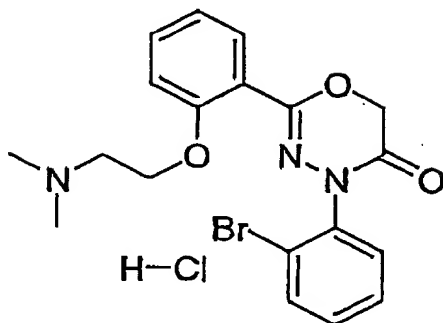
 Ca^{2+} 

MW 277.28

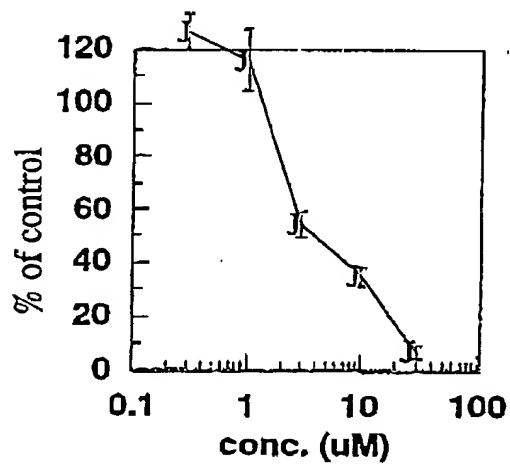
 $[\text{Ca}^{2+}]_i$ (IC_{50} , μM) 2.28

Sample No. 187

Structure

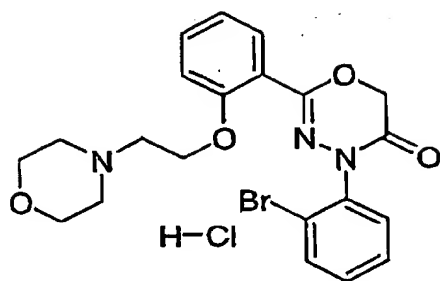
 Ca^{2+} 

MW 454.75

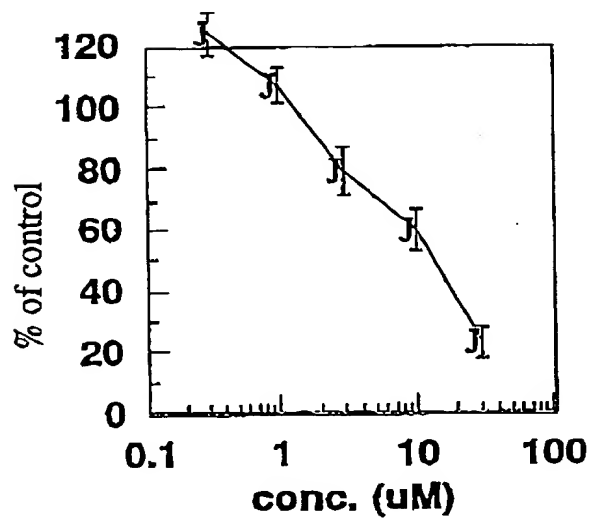
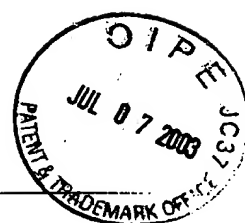
 $[\text{Ca}^{2+}]_i$ (IC_{50} , μM) 4.14

Sample No. 188

Structure

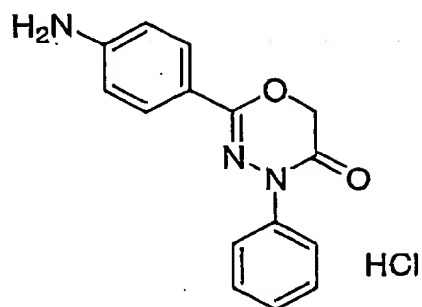


MW 496.79

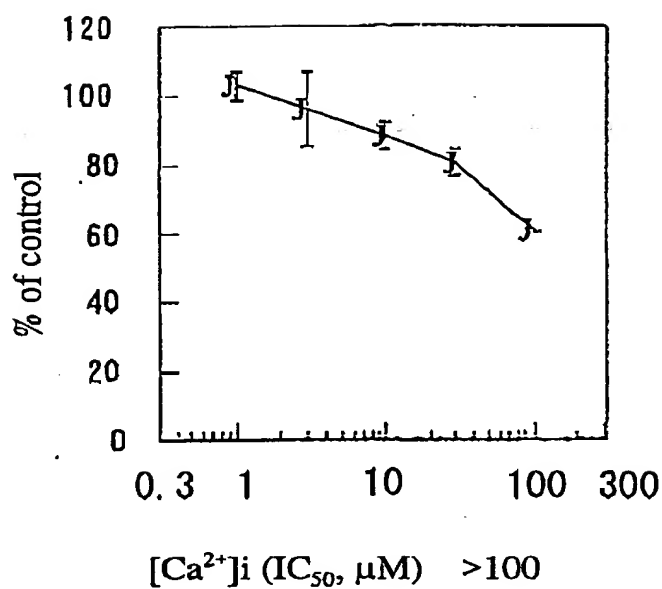
 Ca^{2+}  $[\text{Ca}^{2+}]_i$ (IC_{50} , μM) 11.10

Sample No. 044

Structure

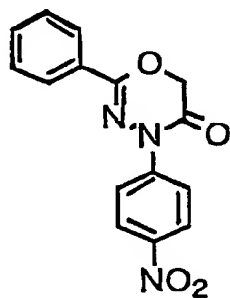


MW 303.75

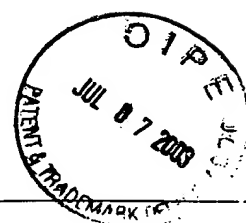
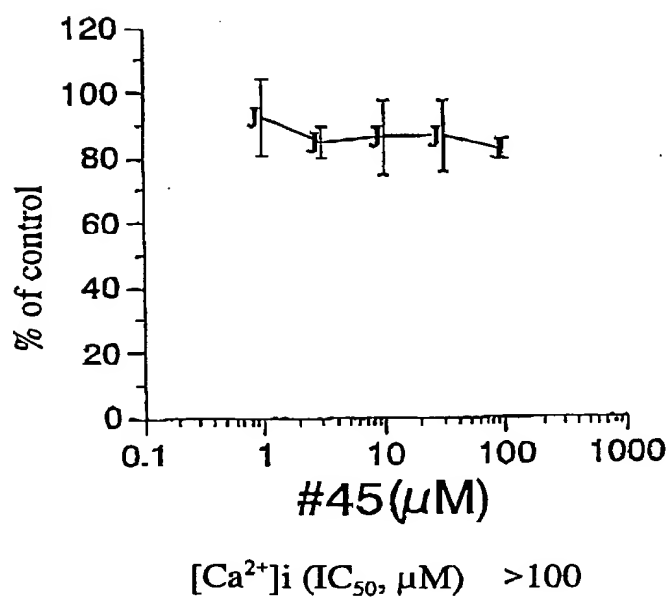
Ca²⁺

Sample No. 045

Structure

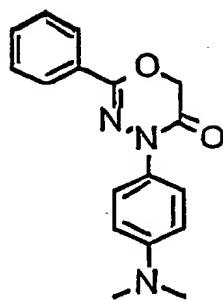


MW 297.27

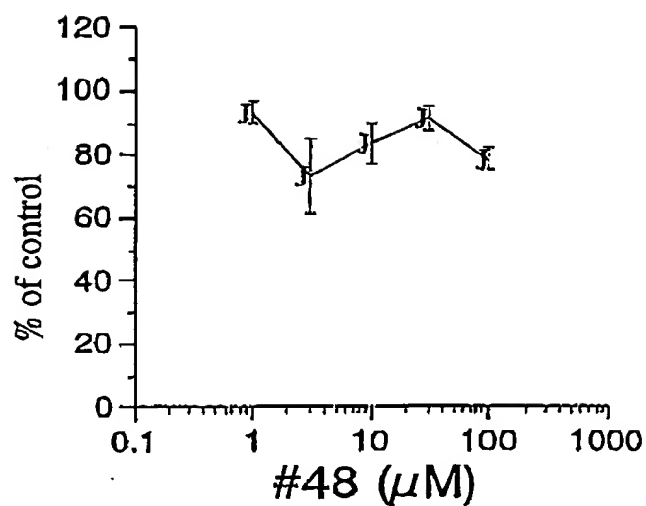
Ca²⁺

Sample No. 048

Structure

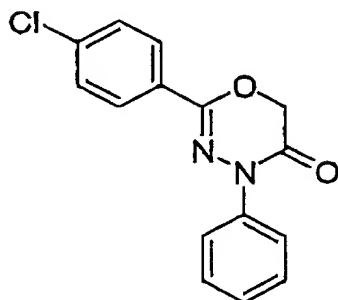
 Ca^{2+} 

MW 295.34

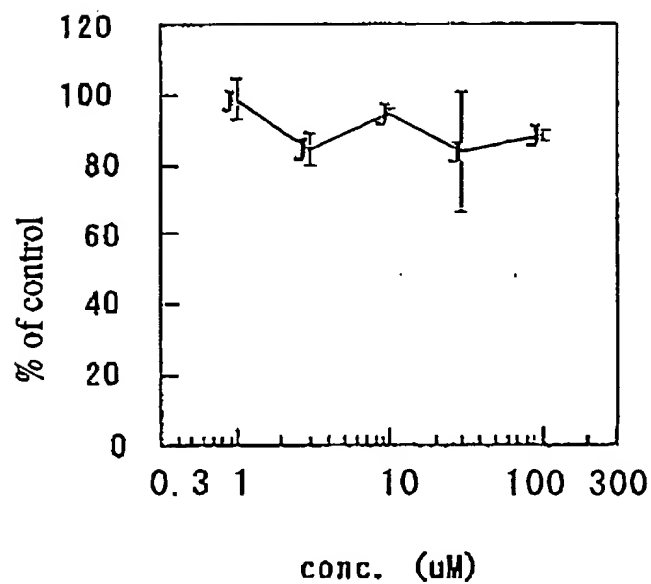
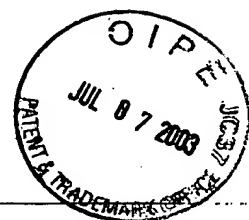
 $[\text{Ca}^{2+}]_i$ (IC_{50} , μM) >100

Sample No. 068

Structure

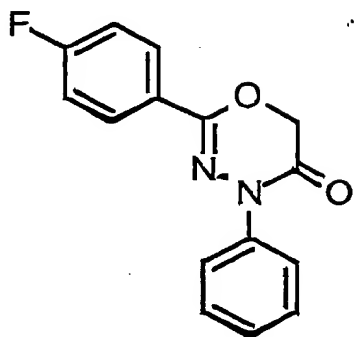
 Ca^{2+} 

MW 286.72

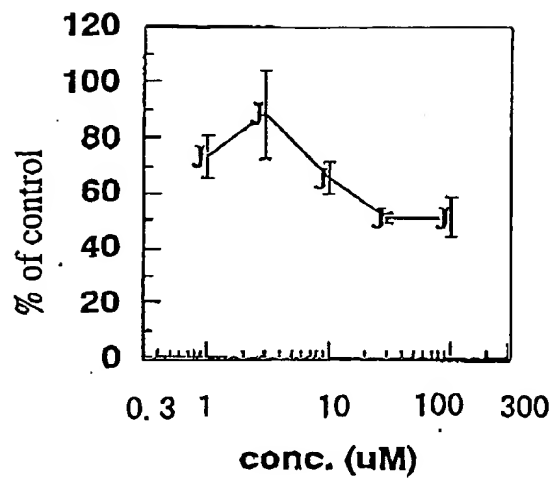
 $[\text{Ca}^{2+}]_i$ (IC_{50} , μM) >100

Sample No. 114

Structure

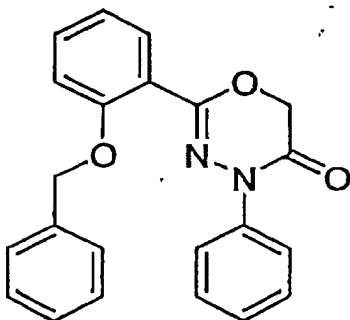
 Ca^{2+} 

MW 270.26

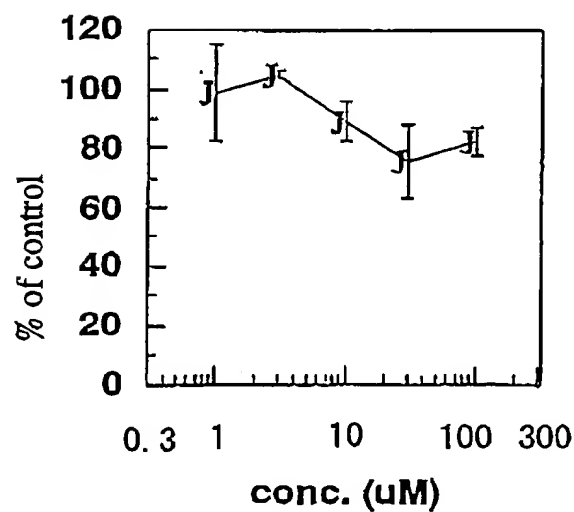
 $[\text{Ca}^{2+}]_i$ (IC_{50} , μM) >100

Sample No. 132

Structure

 Ca^{2+} 

MW 358.40

 $[\text{Ca}^{2+}]_i$ (IC_{50} , μM) >100